Abuse-Deterrent Opioids – Evidence Evaluation & Labeling

Medication: MorphaBond ER® (morphine extended-release)

Evaluation Date: 5/18/17 Evaluation History: ☒ Initial Version 1.0, or ☐ Version _____

Current Product Labeling established: ☐ Prior to or ☒ After publication of FDA Guidance to Industry Document (4/2015)

This is a: (Check all that apply)

- ☒ New product
- ☐ Existing product, new formulation
- ☐ Existing product with new/updated labeling
- ☐ Other: _____

Product Abuse Deterrent Property Classification: – Check all that apply

- ☒ Physical / Chemical barrier
- ☐ Agonist / Antagonist combination
- ☐ Aversion
- ☐ Delivery System
- ☐ New Molecular entity or Prodrug
- ☐ Combination (check combined items)
- ☐ Novel Approach

Product Labeling:

Does the product have FDA abuse deterrent labeling? ☒ Yes or ☐ No Year obtained: 2015

Abuse Deterrent Evidence provided. Summary of in-depth literature review and product evaluation based on FDA Guidance to Industry Document

☒ Laboratory-based in vitro manipulation and extraction studies (Category 1)

Description of Research: *In vitro* data indicates tablets are resistant to crushing and cutting using most household tools, attempts to dissolve causes formation of viscous gel that is difficult to syringe, and extraction in large and small volumes of solvent is results in low yields.

☒ Pharmacokinetic Studies (Category 2)

Description of Research: Pharmacokinetic studies indicate crushed MorphaBond ER® tablets given intranasal results in a 49% lower peak plasma concentration (C_{max}) of morphine and 68% lower C_{max} of morphine-6-glucuronide (M6G) compared to crushed intranasal MS Contin®. In addition, crushed intranasal MorphaBond ER® resulted in 75% lower exposure after 30 minutes ($AUC_{0\text{-}0.5h}$) for morphine and 68% lower $AUC_{0\text{-}0.5h}$ for M6G compared to crushed intranasal MS Contin®

☒ Clinical Abuse potential studies (Category 3)

Description of Research: Intranasal clinical abuse potential study assessed peak drug liking on VAS as primary endpoint. Peak drug liking for crushed intranasal MorphaBond ER® was significantly lower compared to crushed intranasal MS Contin® (P<0.0001). In addition, there was no significant difference in drug liking between crushed intranasal MorphaBond ER® and intact MorphaBond ER® taken orally (P=NS).

☐ Clinical Abuse potential studies (Category 3)

Description of Research: _____

☐ Clinical Abuse potential studies (Category 3)

Description of Research: _____

☐ Additional Studies / Post Market data which assessed the impact of abuse-deterrent formulation (Category 4)

☐ Post market

☐ Formal studies included recommended study design features (see page 19 FDA Guidance document)
Description of Research: _____
_____

☐ Determination if use of product results in meaningful reductions in abuse, misuse, and related adverse clinical outcomes, including addiction, overdose, and death
Description of Research: _____
_____

☒ Outcome Measures and Data Interpretation in Abuse Potential Studies

- Standardized Instruments

☒ Visual Analogue Scales (VAS)
Description of Research: Drug liking, take drug again, Drug Effects Questionnaire.
_____

☐ Profile of Mood States
Description of Research: _____
_____

- Data Interpretation

☒ Primary Analysis
Description of Research: Comparison of mean maximum effect (E_{max}) between crushed intranasal MorphaBond ER® and crushed intranasal MS Contin®

☒ Statistical Analysis
Description of Research: Provided descriptive statistics; followed FDA guidance to industry on statistical analysis for abuse-deterrence studies based upon comparison of mean drug liking VAS and percent reduction of drug liking VAS.

☒ Data and dropout for non-completers
Description of Research: Data regarding dropout and non-completers accounted for.

☐ None of the above

Strength of Evidence of Abuse Deterrent Properties:

☐ Evidence is based on physical/chemical property, theoretical assumptions or manufacturer's claims and is not yet supported by scientifically sound outcome data which demonstrates a reduction in the abuse of the product in the community setting compared to levels of abuse, overdose, and death that occurred when only formulations of the same opioid without abuse-deterrent properties were available (Category III)

☒ Evidence is based on physical/chemical property, clinical abuse potential studies or laboratory manipulation studies and is not yet supported by scientifically sound outcome data which demonstrates a reduction in the abuse of the product in the community setting compared to levels of abuse, overdose, and death that occurred when only formulations of the same opioid without-abuse-deterrent properties were available (Category II)

☐ There is evidence, supported by scientifically sound outcome data, which demonstrates a reduction in the abuse of the product in the community setting compared to levels of abuse, overdose, and death that occurred when only formulations of the same opioid without abuse-deterrent properties were available (Category I)